B1 thereby inhibit the interaction of said G protein and CD14, such that septic shock in the subject is treated.

REMARKS

Claims 1-17 were pending in the application. Claims 11-17 have been canceled herein. In addition, claim 1 has been amended. Accordingly, claims 1-10 remain pending in the instant application.

No new matter has been added. Support for the amendments to claim 1 can be found throughout the instant specification. The amendments to the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

For the Examiner's convenience, a copy of the pending claims is attached hereto as Appendix A. Also attached hereto is a marked-up version of the changes made to the specification and the claims by the current amendments. The attached page is captioned "Version With Markings to Show Changes Made".

Withdrawal of Certain Rejections

Applicants gratefully acknowledge that the following rejections and objections have been indicated as withdrawn:

1. The rejection under 35 U.S.C. § 119(e) has been withdrawn.
2. The objection to the specification due to the presence of informalities has been withdrawn.
3. The rejection of claims 1-3, 6-9 and 11-14 under 35 U.S.C. § 102(b) as being anticipated by Bertics *et al.* has been withdrawn.
4. The rejection of claims 10 and 17 under 35 U.S.C. § 103(a) as being obvious over Bertics *et al.* has been withdrawn.
5. The rejection of claims 1-3, 6-9 and 11-14 under 35 U.S.C. § 102(b) as being anticipated by Proctor *et al.* has been withdrawn.
6. The rejection of claims 11 and 14-16 under 35 U.S.C. §102(b) as being anticipated by Solomon *et al.* has been withdrawn.

Rejection of Claims 5 and 16 Under 35 U.S.C. § 112, second paragraph

The Examiner has maintained the rejection of claims 5 and 16 under 35 U.S.C. § 112, second paragraph, as being indefinite because the term "analog" is not defined either in the description or the art. It is the Examiner's opinion that "[i]t is not clear what degree of functional or structural similarity is necessary for one compound to be considered an analog of another compound."

Applicants respectfully traverse and request reconsideration. Applicants respectfully reiterate that the ordinarily skilled artisan would recognize that the term "analog" refers to a compound which is *structurally similar* to a specified compound, *and* has the *same or substantially the same activity* as the specified compound, but differs slightly in composition. Applicants specifically incorporate by reference various mastoparan "analogs" known in the art (see page 8, lines 4-6, of the specification wherein Applicants incorporate by reference U.S. Patent No. 5,589,568). Applicants respectfully note that these mastoparan analogs are all structurally and functionally similar to mastoparan. Thus, contrary to the Examiner's assertion, the term "analog" is sufficiently definite based on both the meaning provided by Applicants' disclosure and the meaning understood in the art.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 5 and 16 under 35 U.S.C. § 112, second paragraph.

Rejection of Claims 1-9 and 11-16 Under 35 U.S.C. § 102(b)

The Examiner maintains the rejection of claims 1-9 and 11-16 under 35 U.S.C. § 102(b) as being anticipated by Higashijima *et al.* Specifically, the Examiner is of the opinion that "[w]ith respect to claims 1-9, because the same active agent is being administered to the same subject by the same method steps, inherently septic shock will be prevented in Higashijima *et al.* to the same extent claimed by Applicants. With respect to claims 11-16, a suggested use limitation does not impart novelty or non-obviousness to a composition claim where the composition is otherwise taught or suggested by the prior art."

Applicants respectfully traverse and request reconsideration. However, in the interest of expediting prosecution, Applicants have canceled claims 11-17 directed to compositions. Accordingly the rejection is moot as it pertains to these claims. In addition, Applicants have amended claim 1 such that the currently pending claims 1-10 are directed to a method of treating septic shock which the Examiner acknowledges is not taught by Higashijima *et al.*

Specifically, Higashijima *et al.* teach methods and compositions for modulating the action of G proteins through mastoparans and mastoparan analogs. Applicants emphasize that contrary to the Examiner's assertion, one of ordinary skill in the art would not have used Higashijima *et al.*'s methods to treat septic shock. The only diseases mentioned in Higashijima *et al.* are asthma, ulcers, cardiovascular diseases and Parkinson's disease. Applicants were the first to demonstrate that G proteins are involved in septic shock. Furthermore, Applicants were the first to demonstrate that LPS mediated toxicity (which results in sepsis) is caused by the interaction between CD14 (the LPS receptor) and G proteins. Thus, without the benefit of Applicants' disclosure, the ordinarily skilled artisan would not have had the requisite knowledge to have used the methods and compositions of Higashijima *et al.* to treat a patient with septic shock.

Accordingly, Applicants request reconsideration and withdrawal of the rejection of claims 1-9 and 11-16 under 35 U.S.C. § 102(b).

Rejection of Claims 1-9 and 11-16 Under 35 U.S.C. § 102(b)

The Examiner maintains the rejection of claims 1-9 and 11-16 are under 35 U.S.C. § 102(b) as being anticipated by Cabeza-Arvelaiz *et al.* Specifically, the Examiner is of the opinion that "[t]he Cabeza-Arvelaiz *et al.* article teaches the use of pertussis toxin and cholera toxin to inhibit the effects of LPS. The toxins antagonize LPS activation of G proteins. . . .The toxins constitute analogs of mastoparan because of the toxins have the same function and effect as mastoparan in treating or prevent septic shock, and because the claims do not set forth any structural limitations on what constitutes an analog of mastoparan."

Applicants respectfully traverse and request reconsideration. In order to expedite prosecution, Applicants have canceled claims 11-17, thereby rendering this rejection moot as it pertains to those claims. With respect to claims 1-9, Applicants submit that

Cabeza-Arvelaiz *et al.* merely teach that pertussis toxin and cholera toxin are capable of inhibiting the effects of LPS. This reference does not teach each and every element of the claimed method, *i.e.*, a method for treating or preventing septic shock in a subject comprising administering to the subject an effective amount of an agent which binds G protein, to thereby inhibit the interaction of said G protein and CD14, such that septic shock in the subject is treated or prevented. Cabea-Arvelaiz *et al.* do not teach that the interaction of the LPS receptor, CD14, and G proteins must be inhibited to modulate LPS mediated toxicity. As the Examiner is aware, to anticipate a claim, the reference must teach each and every element of the claim. Here, the cited reference fails to do so.

Moreover, Applicants respectfully emphasize that pertussis and cholera toxins do not fall under the scope of the term "analog of mastoparan" as referred to in the pending claims and the instant specification. As set forth above, the term "analog" is an art-recognized term referring to a compound which is *structurally similar* to a specified compound, *and* has the *same or substantially the same activity* as the specified compound, but differs slightly in composition. In contrast, pertussis and cholera toxins are not structurally similar to mastoparan and thus do not fall within the ambit of the term "analog." Applicants therefore submit that based on the teachings of the instant specification and the general knowledge in the art, the ordinarily skilled artisan would have known that pertussis and cholera toxins are not mastoparan analogs.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-9 and 11-16 under 35 U.S.C. § 102(b).

Rejection of Claims 10 and 17 Under 35 U.S.C. § 103(a)

The Examiner rejects claims 10 and 17 under 35 U.S.C. § 103(a) as being obvious over Cabeza-Arvelaiz *et al.* Specifically, the Examiner is of the opinion that "[t]he Cabeza-Arvelaiz *et al* article teaches that antibiotic treatment is a current therapy for LPS-induced shock, but does not teach the combination of an antibiotic with the toxin. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to use a combination of the antibiotic and toxin taught by the Cabeza-Arvelaiz *et al.* article to treat gram negative bacteria infection because it is prima facie obvious to use a combination of treatments where each treatment has been

used individually to treat the same disease and where there is no indication of negative interaction between the treating agents."

Applicants respectfully traverse and request reconsideration. In the interest of expediting prosecution, Applicants have canceled claim 17 thereby rendering the instant rejection moot as it pertains to this claim. With respect to the rejection of claim 10, as set forth above, Applicants respectfully reiterate that Cabeza-Arvelaiz *et al.* merely teach that pertussis toxin and cholera toxin are capable of inhibiting the effects of LPS without teaching each and every element of the claimed method. Moreover, Applicants reiterate that Cabeza-Arvelaiz *et al.* specifically state that although the antibiotic pentoxifylline (an agent which inhibits turn-over of cAMP) has been found to be able to prevent sepsis, which suggests that the cAMP pathway is of critical importance in lethal LPS-induced pathology, their own work did not corroborate this suggestion since cAMP-raising agents used in their work failed to mimic the effects of the toxins they showed inhibited LPS-mediated toxicity (page 133, paragraph 6). This is the only reference to antibiotics made Cabeza-Arvelaiz *et al.* Accordingly, contrary to the Examiner's assertion, Cabeza-Arvelaiz *et al.* teach away from using antibiotics in conjunction with methods and compositions of the invention used for treating or preventing septic shock in a subject. Thus, this reference does not provide the motivation, suggestion or expectation of success for treating septic shock by including an antibiotic with the methods and compositions of the invention.

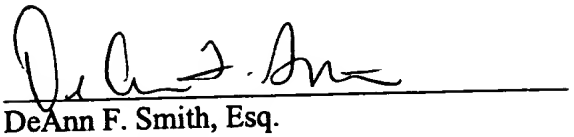
Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 10 and 17 under 35 U.S.C. § 103(a).

CONCLUSION

Reconsideration and allowance of all the pending claims is respectfully requested. If a telephone conversation with Applicants' attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call Applicants' attorney at (617) 227-7400.

Respectfully submitted,

LAHIVE & COCKFIELD, LLP



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Dated: **April 29, 2002**

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 11-17 were canceled.

Claim 1 was amended as follows:

1. **(Amended)** A method for treating ~~or preventing~~ septic shock in a subject comprising administering to the subject an effective amount of an agent which binds G protein, to thereby inhibit the interaction of said G protein and CD14, such that septic shock in the subject is treated ~~or prevented~~.